Boolean network models display graphs that show nodes, which represent genes, gene products, or input compounds, where each can be represented as on or off using 1’s and 0’s respectively. The state of the node is determined by Boolean expressions which use the on/off state of the nodes pointing to or inhibiting the node. There is a variety of methods that researchers use to operate Boolean networks, including truth tables, stochastic models, and threshold models to name a few.

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A few possible applications of these methods are fields of study, such as cancer research, and signaling network research, and showing possible knockout effects. Another application is the ability to run simulations to determine new pathways, which will allow for research to become more detailed and sophisticated.

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The genetic modification of E. coli has a large impact on the medical field. The first useful outcome of the genetic modification of E. Coli was the production of insulin. Since then, researchers have been producing other useful medicines, such as morphine, hydracodone, and many vaccines.

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Our research project is based on the work done by Bioengineers at Kyoto University. Their research focused on modifying E. coli to produce opioid precursors. The findings from this research revealed that by manipulating 4 strains of E. coli they are able to produce Thebaine. They modified the genetic material of E. Coli using genes from other bacteria and enzymes from two opium poppies to get these results. Manipulating 2 more genes from here allowed them for the creation of hydracodone.

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The model used for our code follows the engineering of E. coli to produce hydracodone pathways. In total there are 14 nodes that represent each of the intermediates that are present in the pathways. The edges that are created for these nodes are all ‘+’ edges which indicate that each edge connects proceeds down the pathway in order.

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In our program we modeled the Boolean network for E. coli, and ran a simulation using truth tables to determine the outcome. We used file input and output to make modeling the data easier, and allowed us the ability to save each type of graph and model we produced.

One Next Slide: This image displayed shows the pathway and how each of the chemicals links in order until hydracodone is produced. Our particular pathway is the one represented in blue.

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Our program is a simplistic Boolean network modeler which allows us to fulfill this list of goals. We wanted our program to generate the Boolean network graph, allow for user input to determine the transition of the pathways, run a simulation given a vector of nodes, display the results in graph form, use file I/O to allow the model to be re-ran without a complete re-entry of the data, and allow nodes to simulate more complex network interactions.

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The Boolean functions that we used are summations that add up all of the nodes. From there a system of equations is used to determine whether or not the node will be given 1 or 0.

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Displayed here are some of our example test files. The top line is the nodes that will be used. The next few lines determine the action that will be taken by the node. After that a definition of the sigma function is set up.

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Simulations for a small network:

A small test model that we used to illustrate the model of a lac operon.

Next slide: This graph shows the lac operon model using inducers, repressors, promoters, and operators.

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Here we have the graphs of each node over 10 generations.

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The modified E. coli model.

Next Slide: Our network, which is the production model for hydracodone, has 14 nodes is seen here, and each node is connected to the next part of the pathway.

Some possible improvements include adding in more pathways that use common chemical intermediates, which will make the model more realistic. This could be integrating the model network with other already developed E. coli networks. We could allow for asynchronous updating of the nodes which would regulate their update speed. We could allow for user input to perform mid-model node deletion in order to model possible mutations. Finally we could create our own graph generation functions that would handle the self-directed edge visualization in the graphs.